REMARKS

The Official Action dated October 21, 2005 has been carefully reviewed. In view of the amendments submitted herewith and the following remarks, favorable reconsideration and allowance of this application are respectfully requested.

At the outset, it is noted that the Examiner has rejoined claims 40-44, 66-68, 99 and 103 (Group II claims) with the elected set of claims of Group I (claims 33-39, 60-65, 69-83, 100, 101, with claims 93-98, 102 and 104-110 having been acknowledged by the Examiner as linking the claims of Group I and now rejoined), such that the claims now pending and subject to examination in this application are claims 33-44, 60-80, 83 and 93-110, and the species under consideration is the application of these claims to plants. All claims under examination stand rejected.

As another preliminary matter, Applicants respectfully request that the Examiner clarify the status of claim 45. The Examiner has indicated that the Groups I and II inventions have been rejoined yet indicates that claim 45 has been withdrawn from consideration. Inasmuch as claim 45 was listed in the claims directed to the Group II invention, Applicants respectfully submit that its withdrawal from consideration in is error.

The Examiner has requested that the specification be amended to recite the status of the parent application. The specification has been amended in keeping with the Examiner's request. Applicants have also omitted the incorporation by reference statement in the priority claim. Additionally, a PTO/SB/08B form is submitted herewith listing the references provided on the 892 form in the IDS filed on June 30, 2004.

At page 4 of the Official Action, the Examiner contends

the abstract is too long and does not refer to the invention presently claimed. Applicants submitted an amended abstract with the preliminary amendment filed on March 22, 2004 and therefore this objection is inappropriate. However, Applicants have again amended the abstract, thereby rendering this objection moot.

The Examiner has objected to claims 75, 77, 97, 102 and 108 as being of improper dependent form for failing to limit the subject matter of a previous claim. These claims have been amended to clearly limit the subject of the previous claims thereby removing this ground of objection.

Claims 33, 35, 40-44, 75, 77, 78, 93-110 stand rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter regarded as the invention.

At page 9 of the Official Action, the Examiner has rejected claims 33-44, 60-80, 83 and 93-110 under 35 U.S.C. §112, first paragraph asserting that undue experimentation would be required to practice the subject matter encompassed by the claims.

The Examiner has raised a provisional double-patenting rejection of claims 33-44, 60-80, 83 and 93-110 under 35 U.S.C. §101 asserting that these claims are identical to those presented in US Patent Application 11/013,469. It is respectfully requested that this rejection be held in abeyance pending the notification of allowable subject matter.

Claims 33, 35, and 37-44 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Hamilton et al. Plant J. 15:737-746 (1998).

The foregoing objections and rejections constitute all

of the grounds set forth in the October 21, 2005 Official Action for refusing the present application. Each of these objections and rejections are traversed for the reasons set forth below.

THE CLAIMS AS AMENDED FULLY COMPLY WITH THE REQUIREMENTS OF 35 U.S.C. §112, SECOND PARAGRAPH

The Examiner has rejected claims 33, 35, 40-44, 75, 77, 78 and 93-110 as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter regarded as the invention.

The relevant inquiry in determining whether a given claim satisfies the requirements of 35 U.S.C. §112, second paragraph, is whether the claim sets out and circumscribes a particular area with a reasonable degree of precision and particularity such that the metes and bounds of the claimed invention are reasonably clear. In re Moore, 169 U.S.P.Q. 236 (CCPA 1971). Applicants respectfully submit that with respect to the claims as amended, such inquiry must be answered in the affirmative. Applicants' response to these grounds of rejection are set forth below:

Claims 33 and 40 are said to be indefinite because the recitation of "silencing agent" in the specification at page 8 discloses: "'Silencing agent' in this context may be one or more of an inducer, signal, or specificity determination of gene silencing, particularly PTGS. Preferably this will be a SARM (as opposed to a SSRM)." The Examiner further contends that the term "may" is open language, and that this "recitation can therefore encompass other things." In response, the Examiner's attention is respectfully directed to the passage at page 8, lines 15 to 21, wherein it is

stated "The process described above may form part of a more extensive process for producing or isolating a **silencing agent** for a target gene, which silencing agent is a preferably a SRM, the process comprising the steps of: (i) silencing a target gene in an organism, (ii) performing a process as described above in order to isolate a SRM appropriate for that gene." At page 2 of the specification, SRMs are defined as RNA molecules "of a uniform length, estimated at around 25 nucleotides"... comprising "short sense and antisense RNA molecules (hereinafter, collectively, SRMs)". Claim 33 has been further amended to recite that the SRMS can form base pairs, e.g., specifically hybridize with the target RNA. Support for this amendment can be found at page 2, lines 28 to 33 and at page 23, lines 26 to 39. As an additional matter, Applicants take exception to the Examiner's contention at page 6 of the Official Action that "claim 60 does not encompass SRMs whose sequences are complementary to the gene encoding the gene product" given the clear teaching in the specification.

Accordingly, Applicants strenuously submit claims 33 and 40 expressly recite, and provide a clear definition of the subject matter encompassed by the phrase "silencing agent" in conjunction with the term SRM. It should therefore be of no import that the specification indicates that the silencing agent may take one of a number of specifically recited forms.

In light of the definition of SRMs provided in the specification, it is respectfully submitted that the metes and bounds of the recitation of "silencing agent" would be clear to one of skill in the art. Reconsideration and withdrawal of this ground of rejection is therefore, respectfully requested.

The Examiner contends that the recitation of the phrase "silencing agent comprises short RNA molecules" renders claims 35, 41 and 42 indefinite. The Examiner is unclear at to what kind of silencing agents can "comprise short RNA molecules". As explained above, SRMs, (e.g., short complementary sense and antisense molecules) are effectors of gene silencing. It is urged again that the claim is definite on its face in light of the disclosure in the specification and thus the rejection of these claims under 35 U.S.C. §112, second paragraph is improper and should be withdrawn.

Claim 75 allegedly lacks clarity for inclusion of the phrase "target gene is expressed by a virus, parasite or predator of an organism containing said target gene". The Examiner is unclear as to exactly where the target gene is located. Claim 75 has been amended to make it clear that the target gene of the virus, parasite or predator is contained within the plant cell of base claim 71.

Claims 77, 100 and 109 are allegedly unclear for the recitation of "the recitation "said SRM comprises short sense and antisense molecules complementary to a sequence contained in a gene that encodes said gene product". The Examiner contends that it is unclear how the SRM can contain both sense and antisense molecules. However, as expressly disclosed in the specification, the term SRM encompasses both SSRMs and SARMs which correspond to each other and are complementary. That is, the SRMs are double stranded. The Examiner is also unclear as to "how sense and antisense sequences can both be complementary to the same sequence in the gene." However, with respect to a mRNA, the SARMs are complementary to the target, while, with respect to the gene encoding the mRNA, the SSRMs are complementary to one strand while the SARMs are complementary to the other strand of the

target gene. Accordingly, Applicants respectfully submit that these claims are not indefinite.

In claim 93, it is stated that the recitation "characterized as" in line 5 renders the claim indefinite as to whether the objected to language implies "comprising" or "consisting of" language. Claim 93 has been amended to eliminate the objectionable language. The Examiner is also unclear whether the SRM consists of, or comprises 25 nucleotides plus or minus 1, 2, 3, 4, or 5 nucleotides. As described in the specification, SRMs are of uniformly about 25 nucleotides in length. However, this length can vary slightly by a few nucleotides. It is submitted that the skilled person having the present specification before him would readily comprehend the subject matter encompassed by the phrase "25 nucleotides, plus or minus 1, 2, 3, 4, 5 nucleotides".

The Examiner contends that claim 97 is rendered indefinite for inclusion of the phrase "said target gene is comprised in a virus, parasite or predator affects an organism containing said gene". Claim 97 has been amended to remove this typographical error, thereby removing any perceived indefiniteness from the claim.

Claim 102 is allegedly lacks clarity for the recitation of the phrase "equivalent cell" in line 6 as the Examiner is unclear as to what is considered equivalent. The claim has been amended to clarify the subject matter encompassed by the claim e.g., the silencing agent is introduced into a cell of an organism *in vivo* after having been tested for silencing in a cell of said organism *in vitro*. Additionally, proper antecedent basis is now provided for the recitation of "said cell".

Claims 104 and 105 are allegedly indefinite as the Examiner is unclear as to what cell is referred to. Base claim 102 has been amended to clarify that the selected nucleic acid which induces silencing in vitro can be used in vivo for silencing of that selected nucleic acid.

In light of all the foregoing, it is respectfully submitted that the claims are amended fully comply with the requirements of 35 U.S.C. §112, second paragraph. Accordingly, the rejection of claims 33, 35, 40-44, 75, 78, and 93-110 is improper and should be withdrawn.

THE CLAIMS AS AMENDED FULLY COMPLY WITH THE ENABLEMENT REQUIREMENTS UNDER 35 U.S.C. §112, FIRST PARAGRAPH

A rejection under 35 U.S.C. §112, first paragraph, based on inadequate enablement is proper only when the rejected claim(s) is (are) of such breadth as to read on subject matter to which the specification is not enabling. In re Borkowski, 164 U.S.P.Q. 642 (CCPA 1970). Moreover, it is settled law that whenever the adequacy of enablement provided by an applicant's specification is challenged, the PTO has the initial burden of giving reasons, supported by the record as a whole, why the specification is not enabling. In re Armbruster, 185 U.S.P.Q. 152 (CCPA 1975). Indeed, a properly supported showing that the disclosure entails undue experimentation is part of the PTO's initial burden under §112, first paragraph. In re Angstadt, 190 U.S.P.Q. 214 (CCPA 1976).

Claims 33-44, 60-80, 83 and 93-110 stand rejected as allegedly encompassing subject matter which was not enabled by the disclosure in the specification. While the Examiner

acknowledges that the specification is "enabling for the claimed method when the nucleic acid sequence that is introduced in the cell to cause PTGS is double-stranded or if single-stranded, and is not as small as 30 nucleotides", it is the Examiner's position that the specification "does not reasonably provide enablement for the claimed method with single-stranded SRMs".

From the foregoing, Applicants understand that the Examiner has acknowledged that the specification is enabling with respect to the claims to the extent they encompass SRMs which are double stranded (i.e. comprised of SARMs and corresponding SRMs, as disclosed, for example, at page 2, lines 12-16 of the specification). However, the Examiner appears to be objecting to or rejecting the claims to the extent that they encompass single stranded short RNA effector molecules, whether they be SARMs or SSRMs. Thus, at page 9 of the Official Action, the Examiner notes that the claims "are broadly drawn towards a method of silencing a target gene in an organism (the elected species is plants) by post-transcriptional gene silencing (PTGS), comprising introducing into a plant a silencing agent which targets a targeted region of said target gene, wherein the silencing agent comprising short RNA molecules (SRMs) which are 25 nucleotides long plus or minus 1-5 nucleotides, and which are specific for the targeted region of the target gene, or wherein the SRMs are short anti-sense RNA (SARMs) and/or short sense RNA molecules (SSRMs)".

At page 10 of the Official Action, the Examiner asserts that "SRMs are defined on page 4 as short RNA molecules 25 nucleotides in length, plus or minus 1-5 nucleotides (page 4, lines 4-14). The specification also indicates that, in performing the invention, it may be preferred to utilize

SARMs rather than SSRMs, although it is to be understood that SSRMs can be used whenever SARMs are referenced (page 4, lines 20-25). **This indicates that SRMs are single-stranded RNA molecules that are in sense or anti-sense orientation relative to their target sequence." (Emphasis added).**

Applicants take exception to this characterization of the SRMs of the invention. As expressly recited in the specification at page 2, the term SRM is used as a short-hand for SARMs and their corresponding SSRMs (see lines 15-25) "There have been no previous reports of such short sense and antisense RNA molecules (hereinafter, collectively, SRMs)…Because of their correlation with PTGS and the nature of the molecules (short complementary molecules which could base pair with the target RNAs), they [i.e. SRMs] are believed to represent a signal and/or inducer or activator of PTGS." At page 3, lines 10 to 15, it is disclosed "Importantly, the disclosure herein provides evidence that SRMs may be a common mediator of PTGS in both plants and higher organisms, such as the nematodes discussed in the Examples hereinafter. It was previously known that double stranded RNA induces a similar effect to plant PTGS in nematodes, insects and protozoa". This disclosure makes it clear that, contrary to the above emphasized statement in the Official Action, SRMs encompass double stranded complementary SARMs and SSRMs, which correspond to each other. Where the single stranded species is specifically referred to,(as in reference to a SARM or a SSRM), then that reference is obviously intended to refer to the single stranded species, in contradistinction to use of SRMs, which refers to the SSRMs and their complementary and corresponding SARMs. Moreover, the specification discloses that

Single stranded RNA molecules can effectively mediate gene silencing. The Examiner's attention is respectfully drawn to a manuscript attached hereto entitled "Single stranded antisense siRNAs guide target RNA cleavage in RNAi" Martinez et al. (2002) Cell 110:563-574. See the abstract in its entirety. Thus, Applicants contend that either double stranded or singled stranded RNAs can act as effector molecules for inducing PTGS, a concept which is captured in the claims as originally and in the disclosure as filed. Moreover, the specification clearly enables the use of either, and in particular of SRMs, which are double-stranded sense and antisense molecules of approximately 25 nucleotides, to effect silencing in the target cells. New claims 111-115 have been added which specifies that the SARMs and the SSRMs which are components of the SRMs are present in equal abundance. Support for these new claims can be found at page 23, lines 35 to 40. Applicants note that Examiner acknowledges that this subject matter is enabled.

While strenuously disagreeing with the Examiner's contention regarding the effectiveness of single stranded RNA molecules for the reasons provided above, claims 37, 38, 39, 42, 43, 44 which are directed to single stranded SARMs and/or SSRMs are hereby cancelled without prejudice. Applicants reserve the right file one or more continuing applications on the subject matter encompassed by these claims.

Regarding claim 76, The Examiner states that "the claim indicates that the target gene to be suppressed is involved in parasite resistance. The specification does not teach how one skilled in the art would **use** such a plant produced by the method, since it would be more susceptible to parasites…undue experimentation would be required by one skilled in the art

to make and use the claimed invention."

In response, it is urged that the Examiner appears to be making a utility rejection, which should properly be made under 35 USC §101, rather than an enablement rejection, under 35 USC §112. Those skilled in the art are fully enabled to make that which is claimed - a plant (for the elected species) with a reduced parasite resistance. With respect to utility, as stated by the Examiner, the standard is what those skilled in the art would appreciate by what is taught and claimed in the patent application, not what those without any skill in the art would appreciate. It is therefore suggested that in light of the specification's disclosure and this claim, those skilled in the art would immediately appreciate that a plant with reduced parasite resistance would have the obvious utility of being a perfect test bed for anti-parasitic compounds using hyper-susceptible plants as a screen.

In light of the foregoing remarks and claim amendments, the rejection of claims 33-44, 60-80, 83 and 93-110 is untenable and should be withdrawn.

THE CLAIMS AS AMENDED ARE NOVEL OVER HAMILTON ET AL.

The Examiner contends that the disclosure in Hamilton et al. anticipates the subject mater of claims 33, 35, and 37-34. Applicants respectfully disagree. In order to render claims lacking in novelty, a prior art reference relied on in a §102 rejection must identically disclose each and every element claimed. It is respectfully submitted that claims as amended are novel over Hamilton et al. (Plant J., 1998, Vol. 15, pages 737-746).

Hamilton et al. allegedly teach "transgenic tomato

plants transformed with a tomato ACO1 cDNA operably linked to a promoter, wherein ACO1 expression from the transgene and the homologous endogenous gene was subjected to PTGS (pages 738-740). The ACO1 transgene can be considered to be a silencing agent of the endogenous ACO1, as the instant specification does not precisely define "silencing agent" (see the indefinite rejection above). The tomato ACO1 cDNA corresponds to the endogenous ACO1 gene in the host tomato plant, and so the mRNA transcribed from the cDNA **inherently comprises 25 nucleotides plus or minus 1-5 nucleotides** that are specific for the endogenous ACO1 mRNA transcribed from the endogenous gene."

In response, it is urged that the specification clearly defines the subject matter encompassed by the term SRM and the phrase "silencing agent" as it relates to SRMs and thus the claims are clearly distinguishable from Hamilton et al. Claim 33 requires the use of a specific silencing agent comprising SRMs **"wherein said SRMs comprise SARMs and corresponding complementary SSRMs**. Such a silencing agent is nowhere disclosed or suggested by Hamilton et al. Likewise for claims 35 and 37-39 since those claims depend from claim 33. The rejected claims clearly recite the use of **SRMs** to effect silencing as opposed to a large cDNA construct comprising a full length coding region of ACO (See Figure 1 of Hamilton et al. at page 738). It is well settled that "Words in a reference are construed in light of the relevant surrounding circumstances in each case; reference is good only for that which it clearly and definitely discloses. An ambiguous reference will not support an anticipation rejection. In re Hughes, 145 U.S.P.Q. 467 (CCPA, 1965). In other words, if a reference is ambiguous and can be

interpreted so that it may or may not constitute an anticipation of appellant's claims, an anticipation rejection under 35 U.S.C.§102 is improper. See In re Brink, 164 U.S.P.Q. 247 (CCPA, 1970).

Applicants respectfully submit that Hamilton et al. do not disclose methods wherein a SRM of 25 plus or minus 1, 2, 3, 4, or 5 nucleotides is introduced into a cell to effect gene silencing. Accordingly, the rejection of claims 33, 35, 37-34 under §102(b) is inappropriate and should be withdrawn.

CONCLUSION

It is respectfully requested that the amendments presented herewith be entered in this application as this amendment is believed to clearly place the pending claims in condition for allowance.

In view of the amendments and remarks presented herein, it is respectfully urged that the rejections set forth in the October 21, 2005 Official Action be withdrawn and that this application be passed to issue.

In the event the Examiner is not persuaded as to the allowability of any claim, and it appears that any outstanding issues may be resolved through a telephone interview, or an in-person interview, the Examiner is requested to telephone the undersigned attorney at the phone

number given below to arrange such an interview with all due dispatch in light of the special status of this application.

DANN, DORFMAN, HERRELL AND SKILLMAN
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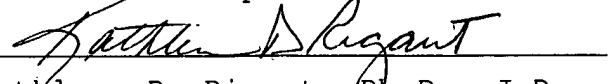
By 

Kathleen D. Rigaut, Ph.D., J.D.
PTO Registration No. 43,047

Telephone: (215) 563-4100
Facsimile: (215) 563-4044
Enclosures: Amended Abstract
Martinez et al.